（書式１８）課程博士

学　位　論　文　要　約

博士論文題目　High fructose-induced hypertension and renal damage were exaggerated in Dahl salt-sensitive rats: Effects of renin-angiotensin system inhibitors and chronic exercise training (Dahl 食塩感受性ラットにおける高フルクトースによる高血圧と腎障害：レニンーアンジオテンシン系阻害薬と長期的運動の効果)

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Background: High-fructose (HFr) was reported to induce metabolic syndrome, salt-sensitive hypertension and multiple organ damage. However, it has been unknown whether the HFr-induced hypertension and renal damage were exaggerate in subjects with salt sensitivity. Chronic exercise (Ex) has antihypertensive and renal protective effects in HFr-fed rats. Thus, impacts of HFr on blood pressure, renal damage and renal renin-angiotensin system (RAS) were tested in Dahl salt-sensitive (DS) and salt-resistant (DR) rats. Furthermore, effects of RAS inhibitors and Ex on the HFr-induced hypertension and renal damage were also examined in DS rats.

Methods: Six-week old, male DS rats and DR rats were fed a control diet or a HFr diet (60% fructose) with a normal-salt content (1.25%) for 12 weeks. Systolic blood pressure (SBP) was measured every 2 weeks. After 12 weeks, plasma and urinary parameters, renal histology and renal expression of RAS components were examined. Furthermore, effects of enalapril (10mg/kg/day), candesartan (1mg/kg/day) and Ex (20 m/min, 0 degrees, 60 min/day, 5 days/week) were examined in DS rats fed the HFr diet.

Results: HFr elevated SBP in DS rats but not in DR rats. HFr increased urinary albumin and liver type-fatty acid binding protein excretions in both rats, but the excretions exaggerated in DS rats. HFr increased plasma lipids and uric acid in both rats, whereas HFr increased creatinine clearance in DS rats but not DR rats. Although HFr decreased plasma renin activity and angiotensin II level in DS rats, HFr-induced glomerular injury, afferent arteriolar thickening and renal interstitial fibrosis exaggerated in DS rats compared with DR rats. HFr increased the renal expression of angiotensinogen(AGT), renin, (pro)renin receptor ((P)RR), angiotensin converting enzyme (ACE) and angiotensin II type 1 receptor (AT1R) in DS rat, whereas HFr increased only ACE expression and decreased the renin and AT1R expressions in DR rats. Enalapril, candesartan and Ex attenuated the HFr-induced hypertension, albuminuria, glomerular hyperfiltration and renal damage in DS rats.

Conclusion: Compared with DR rats, HFr-induced hypertension and renal damage exaggerate in DS rats via renal RAS activation, which can be controlled by RAS inhibitors and Ex.